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Human health effects associated with the commercial use of grunerite asbestos (amosite): Paterson NJ, Tyler TX, Uxbridge UK

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Abstract

Grunerite asbestos (amosite) has been shown in epidemiological and experimental animal studies to cause lung cancer, mesothelioma and pulmonary fibrosis commonly referred to as asbestosis. An overview of the human and experimental animal studies describing the health hazards of grunerite asbestos (amosite) is presented. Of the many human studies describing the heath hazards of asbestos only three factories using mainly, if not exclusively, grunerite asbestos (amosite) have been studied. The first is a series of reports on a cohort of 820 workers from a plant located in Paterson, NJ. Among this cohort, 18.7% died of lung cancer and 17 mesotheliomas occurred. The Paterson factory closed in 1954 and moved to Tyler, Texas where it operated until 1972. Among the 1,130 former workers in the Tyler plant 6 mesotheliomas were reported with 15.8% lung cancer mortality. The third grunerite asbestos (amosite) exposed cohort was an insulation board manufacturing facility in Uxbridge, United Kingdom. Here 17.1% of the workers died of lung cancer and 5 mesotheliomas occurred. The lung content from 48 Uxbridge workers was analyzed by analytical transmission electron microscopy for mineral fibers. The relationship between grunerite asbestos (amosite) concentrations in the lung correlated with grades of fibrosis and asbestos bodies and was lower than the concentration found in the cases with malignant tumors. The lung cancer cases contained more grunerite asbestos (amosite) than mesothelioma cases and in the cases of non-malignant disease the concentrations were lower. In both types of malignancies the concentration of grunerite asbestos (amosite) was very high over a billion fibers per gram of dried lung. Occupational exposure to airborne concentrations of between 14-100 fibers of grunerite asbestos (amosite) per milliliter after 20 year latency causes marked increases in lung cancer, mesothelioma and pulmonary fibrosis (asbestosis).

Keywords: Grunerite asbestos; Amosite; Mesothelioma; Asbestosis

1. Introduction

Asbestos occurs in nature as fine flexible fibers characterized by high thermal stability and high tensile strength (Ross et al., this volume). Asbestos was widely used in the 20th century in the production of various heat resistant materials and fabrics, insulation and friction products and as a constituent of asbestos cement (Alleman and Mossman, 1997; Ross and Virta, 2001).

Most countries regulate six commercial minerals under the asbestos standard. The predominant commercial fiber-type is the serpentine mineral – chrysotile (white asbestos) - while the other five fiber-types are amphibole asbestos minerals. Two of which grunerite asbestos (amosite) (brown asbestos) and riebeckite (crocidolite) asbestos (blue asbestos) were commonly found in commerce in the last century while anthophyllite asbestos and tremolite-actinolite asbestos were much less commonly used (Ross and Virta, 2001). Chrysotile asbestos is the only asbestos fiber-type that continues in commerce. The fibrous particles most commonly associated with taconite are nonasbestos fibrous grunerite although lower concentration of nonasbestos fibrous ferroactinolite has also been reported (Wilson et al., this volume).

We will survey the asbestos-related diseases caused by occupational exposure to grunerite asbestos (amosite) and the relevant *in vivo* and *in vitro* studies to gain some insight about the mechanisms of asbestos-related diseases. This information will provide a background for our goal of describing the health hazards from occupational exposure to grunerite asbestos (amosite) during the manufacturing of products with this asbestos fiber-type. The health hazards in the mining environment are described by Murray and Nelson (this volume).

2. Mineralogical characteristics of grunerite asbestos (amosite)

Amosite asbestos was the geological name given to the mineral by Hall, a geologist, in 1907. He derived the name from the first letters of the mineral's predominant mining region commonly referred to as the **a**sbestos **m**ines **o**f **S**outh Africa with the "ite" commonly given to mineral names (Hall, 1930). To simplify the diverse nomenclature of the many amphibole, minerals names such as amosite, were eliminated in favor of names that denote a specific elemental composition. For amosite the amphibole name with the same elemental composition is grunerite follow by asbestos to denote the crystal form or habit. Amosite or amosite asbestos would continue to be used to describe the mineral in both commerce and the medical literature. We will use both names in this paper.

Grunerite asbestos (amosite) is a fibrous silicate mineral, with the chemical formula $(Fe^{2+}, Mg)_7 Si_8 O_{22} (OH)_2$. Using transmission electron microscopy a narrow range of dimensions has been reported for this asbestos fiber-type. Airborne population of grunerite asbestos (amosite) has been shown to have lengths $\geq$5 µm of 12.7% and 24.6% in mining and bagging respectively (Gibbs and Hwang, 1980) while the width in bulk samples has been reported to be between 0.29-0.35 µm and a little smaller 0.20-0.26 µm for airborne grunerite asbestos (amosite) (Veblen and Wylie, 1993). We have not found any size distribution data for airborne grunerite asbestos (amosite) fibers in the manufacturing environment and there is a paucity of airborne exposure information.

3. Origin of the problem

Early studies of asbestos-related disease at the end of the 19th Century focused on chrysotile asbestos as it was the most widely used asbestos fiber-type. Manufacturing of textiles from chrysotile asbestos was very dusty causing high exposures and a significant incidence of

severe asbestosis (often fatal) developed a few years after first exposure. The first grunerite asbestos (amosite) mine opened at Penge in the Transvaal Province (now referred to as the Northern Province) of South Africa in 1914. Production remained below 5,000 tons per annum until World War II when it increased markedly to over 20,000 tons per annum later peaking at 106,000 tons per annum around 1973. After 20 years of latency these exposures would produce readily detectable asbestos-related diseases in those occupationally exposure while fabricating commercial products, leading to health hazard evaluation studies of grunerite asbestos (amosite) and other asbestos fiber types.

4. Mechanisms and experimental studies

The mechanisms by which grunerite asbestos (amosite) exerts its pathophysiologic effects are as yet not entirely known, but aspects of the mechanism are being uncovered nevertheless. Initial attention focused on fiber morphology as the principal determinant of mesothelioma potency based on a series of experiment animal studies indicating fibers >8 µm in length and ≤0.25 µm in width were commonly carcinogenic at high exposures (Stanton et al., 1981). Although these studies have never been shown to be incorrect, the artificial nature of the implantation model and the very high dose used severely limit their usefulness in evaluating human risk and exposure to experiment animals by inhalation (Johnson, 1993; McConnell, 1995; Addison and McConnell, this volume). Nor do the Stanton morphology criteria explain why some fiber-types have little or no carcinogenic potential even at very high concentration in implantation studies or provide useful information on the health hazards of fibers with dimensions different for those proposed by Stanton et al. (1981) particularly fibers of greater diameter (Nolan and Langer, 1993).

Experimental animal studies where the route of administration has been inhalation the physical dimensions of the fibers are important for pathogenicity (Davis et al., 1986; Miller et al., 1999a,b; Searle et al., 1999) , the longer fibers (often consider as those ≥5 µm as a minimum) being the most pathogenic and translocation from the lungs occurs slowly, if at all. Grunerite asbestos (amosite) translocates to extrapulmonary sites, such as omentum and mesentery, but not as rapidly as chrysotile (Dodson et al., 2000; Suzuki and Kohyama, 1991). Translocation, extremely high exposure and acid stability may account for the high incidence of peritoneal mesotheliomas among workers with occupationally exposure to grunerite asbestos (amosite). Conversely, the persistence of long grunerite asbestos (amosite) fibers in the lung, compared to chrysotile, may account for amphiboles greater facility in causing pulmonary diseases (Churg et al., 1989; Hodgson and Darnton, 2000).

More recent studies have focused on the iron in grunerite asbestos (amosite) and its potential to catalyze the formation of oxygen free radicals and cause breakage in DNA strands *in vitro* (Graham et al., 1999; Nejjari et al., 1993; Lund and Williams, 1994). Grunerite asbestos (amosite) has also been shown to modify the local immune response of pulmonary alveolar macrophage neutrophils (Lawrence and Fox, 1993; Graham et al., 1999). Recent studies report changes in fiber length is associated with changes in *in vitro* properties of grunerite asbestos (amosite). Short fibers obtained by grinding have lower potential damage DNA and lower *in vitro* toxicity and are less effective at altering the redox metabolism (Riganti et al., 2003). Simian Virus 40 (SV40) has been shown to cause mesothelioma in hamsters and a role for SV40 as a etiological agent in human mesotheliomas has been suggested by Gazdar et al. (2002) although the result of recent studies suggest this is unlikely (Lopez-Rios et al., 2004; Manfredi et al., 2005).

Among the studies conducted on animals, the most important to consider are those that target the most common route of entry of asbestos fibers into the body – inhalation (Johnson, 1993; McConnell, 1995). Inhalation studies performed on rats, hamsters and other animals indicate grunerite asbestos (amosite) can cause lung cancer, mesotheliomas and pulmonary fibrosis (asbestosis) (Davis et al., 1986; Miller et al., 1999a, b; Hesterberg et al., 1999; McConnell et al., 1999; Webster et al., 1993). Grunerite asbestos (amosite) impedes pulmonary function by decreasing compliance, and increasing tidal volume and resistance in pulmonary function tests of laboratory animals. These changes were both less pronounced and less prolonged than with chrysotile. They were also correlated with a peribronchial granulomatous reaction, but not with fibrosis (Hiett, 1978).

Intratracheal and intrabronchial instillation of suspensions of grunerite asbestos (amosite) into dogs, guinea pigs and rats showed a rapid translocation of the finer fibers from the alveolar spaces to the lung parenchyma and lymph nodes (Oberdöerster et al., 1988; Searl et al., 1999). Grunerite asbestos (amosite) fibers were cleared from the lungs at a slower rate than chrysotile (Churg et al., 1989).

Injecting grunerite asbestos (amosite) directly into the peritoneal cavity of rats caused an increased incidence of peritoneal mesotheliomas (Davis et al., 1986; Miller et al., 1999a) and clear dose response has been reported (Davis et al., 1991).

Feeding studies, however, show different results. Feeding grunerite asbestos (amosite) to hamsters or rats did not cause an increase in gastrointestinal or any other malignancies (NTP, 1983; NTP, 1990). Feeding grunerite asbestos (amosite), as well as taconite tailings, earth and water from Lake Superior containing taconite tailings to rats also failed to show an increase in gastrointestinal cancer or any other malignancies (Hilding et al., 1981).

5. Asbestos-related disease in humans

All asbestos fiber types are pathogenic to humans (Browne, 1994; Huncharek, 1994). Asbestos dust causes short and long term changes in pulmonary function, appearance of cellular atypia and ferruginous bodies in sputum and radiographic abnormalities (Nash and Fortson, 1981 **Should this be updated?**). Ferruginous bodies in sputum are commonly formed on amphibole asbestos and therefore occur more frequently in populations with exposure to these types of asbestos minerals. Short chrysotile can be coated but is not long enough to form ferruginous bodies with the typical beaded appearance and therefore classical ferruginous bodies are not as commonly found after exposure to chrysotile asbestos. Asbestos causes pulmonary fibrosis (asbestosis), lung cancer and both pleural and peritoneal mesotheliomas with a definite dose response (Acheson et al., 1984; Hodgson and Darnton, 2000; Seidman et al., 1986; Heller et al., 1999; Levin et al., 1998).

Asbestos exposure, whether occupational, para-occupational and environmental is the cause of a high percentage of cases of mesothelioma. In males, occupational asbestos exposure is particularly important and the likely explanation for mesothelioma being five-fold more common in US males than females (Price and Ware, 2004). In females, background or nonasbestos related mesotheliomas represent a significantly higher percentage than among males (Wagner et al., 1960; Newhouse and Thompson, 1965a, b; Edward et al., 1986; McDonald and McDonald, 1996).

Exposure to riebeckite (crocidolite) asbestos and grunerite asbestos (amosite) account for the majority of mesothelioma cases in industrialized countries, even though chrysotile is the asbestos fiber-type most commonly used (Wagner, 1986; Roggli and Pratt, 1993; Churg and

Vedal, 1994; Langer and Nolan, 1998; McDonald and McDonald, 1996; McDonald et al., 2001; Morinaga et al., 2001; Neuberger et al., 2003; Dodson et al., 2003). Asbestos has also been implicated in causing laryngeal, esophageal and gastrointestinal tumors (Clemmesen and Hjalgrim-Jensen, 1981; Raffn et al., 1989) although this has not been established (Gamble, this volume). Studies demonstrating grunerite asbestos (amosite) (as well as other types of asbestos) are present in colon tissue from patients with colon cancer and occupational asbestos exposure although causation was not convincingly shown (Ehrlich et al., 1985; Ehrlich et al., 1991).

Exposure guidelines for grunerite asbestos (amosite) have been debated and modified several times over the years and differ from country to country (Health and Safety Executive, 1988; McCullagh, 1980). The current exposure limit recommended by the US Health Research Institute, NIOSH, is 10^5 fibers/m^3 of air (0.1 fibers/mL) for asbestos fibers > 5μm in length with a length to diameter ratio of at least 3:1. The OSHA permissible exposure limit, for the 8 hour time-weighed-average, is the same. The NIOSH recommendations and OSHA regulations are among the strictest in the world although the regulations do not yet address the importance of asbestos fiber-type. Airborne asbestos fibers in the workplace are collected on a membrane filter and imaged by phase-contrast light microscopy to ensure compliance. The morphological criterion eliminates the fibers to narrow to be imaged with the light optics used and shorter than 5 μm in length from the exposure count.

Several studies have shown a gradient in the risk for lung cancer and mesothelioma between different types of asbestos, riebeckite (crocidolite) asbestos and grunerite asbestos (amosite) conveying a greater risk than chrysotile (Acheson et al., 1984; Gardner and Powell, 1986; Wagner et al., 1988; Rees et al., 1999a, b, c; Hodgson and Darnton, 2000) Smoking increases the risk for lung cancer more than tenfold, but does not increase the risk of developing mesothelioma (Acheson et al., 1984; Dufresne et al., 1996).

Not only workers with occupational exposure to asbestos are at risk, para-occupational exposure is an important cause of asbestos-related disease (Wagner et al., 1960; Newhouse and Thompson, 1965a, b; Edward et al., 1996; Rees et al., 1999a, b, c; Browne and Wagner, 2001; Neuberger and Vutuc, 2003). Para-occupational exposures to asbestos may occur through contact with the work-clothes of a family member working in the asbestos industry or through exposure to asbestos containing products, especially the more friable low density type products (Gibbs and Griffiths, 1990). Animal studies show no connection between ingested grunerite asbestos (amosite) and gastrointestinal malignancies. But airborne grunerite (amosite) asbestos, from the clothes of an asbestos worker or the demolition of an asbestos containing house has led to occult asbestos exposure (Yamada et al., 1997).

6. Cohorts occupationally exposed to grunerite asbestos (amosite)

There are three cohorts of workers exposed, mainly, if not exclusively to grunerite asbestos (amosite) whose mortality has been studied. We use the epidemiology reports on these three studies to summarize what is known about the health hazards of this asbestos fiber-type.

The first study establishing the carcinogenicity of grunerite asbestos (amosite) was conducted on a cohort of 820 workers, from a plant in Paterson, NJ (Selikoff et al., 1972; Seidman et al., 1979; Selikoff and Seidman, 1980; Seidman et al., 1986; Ribak et al., 1989). The plant has been reported to have utilized almost exclusively grunerite asbestos (amosite), and the exposure period for the cohort was limited to the workers who started work between June, 1941 and December 1945 (encompassing the entire period the United States was engaged in World War II). The work force was made up of almost entirely of white males who were older than would be

usual for such a work force as the younger men were in the armed forces.

The concentrations of airborne asbestos were never measured in the Paterson factory although it has been estimated at between 14-75 f/mL (see Levin et al., 1998 for a discussion). Seidman et al. (1986) estimate the average exposure at 50f/mL while for risk assessment, Nolan et al. (1999) used 30f/mL as a lower limit for the average exposure. Only workers hired up to 1945 were included in the cohort so by 1975 the latency period had been a minimum of 30 years. Workers in the cohort with asbestos exposure besides the Paterson factory were omitted so the health hazard would relate specifically to the grunerite asbestos (amosite) exposures in the Paterson, NJ factory. Every death in the cohort was traced, and relevant clinical and pathological information was sought (Fig. 1). In the latest update (where 740 deaths had occurred in the Paterson cohort of 820 men cases of mesothelioma were diagnosed, 8 were pleural mesotheliomas and 9 peritoneal (Table 1). The only significant difference between the pleural and peritoneal mesothelioma cases was the mean time worked was longer in the peritoneal group, 25.6 months versus 43.8 months, (range 2-60 months); indicating the nine peritoneal mesothelioma cases are associated with higher exposures. The mean time from first exposure to the mesothelioma diagnosis was 31 years in both groups. Chest pain was the main symptom in the pleural mesothelioma group with death occurring on average 12 months from the time of first symptom while abdominal pain was the main symptom in the peritoneal mesothelioma group with an average of only 8 months survival from first symptom. Pulmonary insufficiency was the immediate cause of death in most pleural cases (7 out of 8) while wasting and inanition was the immediate cause of death in most peritoneal cases (7 out of 9). The Paterson factory closed in 1954 and moves to Tyler, Texas where a cohort 1,130 workers fabricated grunerite asbestos containing products until February 1972 (Table 1 ; Fig. 1 ; Levin et al., 1998). Exposures at the factory are thought to be similar to those of Paterson as both facilities were operated by the same company and used, in some cases, the very same machinery and processes. Unlike Paterson, where no airborne asbestos concentrations were ever made, in Tyler 170 air samples were collected starting in 1967 (13 years after the plant opened and more than 70% of the air sample collected in 1971) and the concentration range was reported to be from 15.9 to 91.4 f/mL (Levin et al., 1998). More detailed exposures specific to various jobs the workers performed are available for 1967, 1970 and 1971 and are shown in Table 2 (Hurst et al., 1979; Johnson et al., 1982). The exposures are not well described by using a range or an average for all the jobs. Job specific exposures fall into three distinctly different concentration ranges. The highest exposures occurs among the workers milling/ fiberizing the asbestos fibers where the mean for the three years was about 90f/mL working in forming or finishing and curing or packing the asbestos exposures were similar about 37.5f/mL and 17.5f/mL respectively (Table 2). Levin et al. (1998) reported the mortality experience for 222 deaths in the cohort. The total cohort experienced an increased standard mortality ratio for cancer of the lung, trachea and bronchus of 277 while those with less than six months of exposure had a slightly lower SMR of 268. Hurst et al. (1979) reports 85% of the Tyler workers had a history of cigarette smoking although it has not been reported if any of the lung cancers occurred in a non-smoker. Six mesotheliomas occurred in the cohort four pleural and two peritoneal (Table 1; Fig. 1). All of the pleural mesotheliomas had latencies of 15 years or more while in three of the four cases the latency exceeded 25 years. In one case the exposure was less than 6 months, two cases the exposures were between 1 and 5 years and in the fourth case the exposure was greater than 5

years. There were three asbestosis deaths (representing 1.4% of the total mortality) about 3.7-fold less asbestosis mortality than in the Paterson factory (Table 1). No information was given concerning the latency or duration of exposure in the two peritoneal mesothelioma cases or the three asbestosis cases.

No information was given about the jobs done by the six workers who developed mesothelioma (or any other asbestos-related disease) it would be particularly important to know if those who worked for a short period of time were employed on job with high exposures to airborne asbestos. For example, if the worker who developed pleural mesothelioma after just six months exposure was milling grunerite asbestos (amosite) with an average exposure of 91.4f/mL his cumulative lifetime asbestos exposure would be 45f/mL years. This is more than 11-fold higher than the 4f/mL years of cumulative exposure a worker would have after working 40 years at the current US exposure level of 0.1f/mL. Six months of exposure at Tyler could produce a cumulative exposure an order of magnitude higher than a 40-year working career by today's standard. Hurst et al. (1979) comment that even using the lowest asbestos for the three years (1967, 1970, and 1971) when the air samples were collected the lowest OSHA exposure limit was 5f/mL. The milling/ fiberizing exposure are on average 19-fold higher. Brief exposure at Tyler could be associated with a high cumulative exposure limit leading to a high risk of asbestos-related disease.

The third epidemiology study focused on the use of grunerite asbestos (amosite) and chrysotile asbestos in a factory fabricating insulation board containing asbestos in Uxbridge, United Kingdom (Acheson et al., 1981). Asbestos exposure at the factory begins in 1947 and ends when the factory closes in 1979. Up to 1973 both grunerite asbestos (amosite) and chrysotile asbestos were used, although for the last six years before the factory closed only grunerite asbestos (amosite) was used (Fig. 1). As the quantities of short-fiber chrysotile asbestos used were small when compared to grunerite asbestos (amosite) and the limited evidence for low exposure to short chrysotile inducing human mesothelioma led Acheson et al. (1981) to conclude it was reasonable to attribute the five mesotheliomas found among the Uxbridge workers to exposure to grunerite asbestos (amosite) (Table 1). Four of the five mesothelioma cases were pleural and a single peritoneal case occurring in an individual with 28 years of both exposure and latency. The four pleural cases had exposures of 4 months, 1 year 7 months, 3.5 years and 9.5 years with latencies of 22 years, 19 years, 24 years and 14 years respectively. A fifth mesothelioma was reported by Acheson et al. (1981) in an individual who starts work at 50 years of age and develops a mesothelioma 11 years later, after a 6 week exposure in the factory. Due the short latency and the brief exposure to grunerite asbestos (amosite) Acheson et al. (1981) concluded the mesothelioma was not related to exposure at the factory.

Exposures prior to 1964 were thought to be as high as 100f/mL and four of the mesothelioma cases were exposed before 1960 to the dustiest operations such as milling or fiberizing the asbestos. Exposure estimates of Acheson et al. 1984 are almost identical to the mean average of 91.4f/mL reported by Hurst et al. (1979) for milling/ fiberizing at the Tyler, Texas factory. In Uxbridge the job histories of the mesothelioma cases were reported and three of the five mesotheliomas occurred among individuals whose job included milling/fiberizing including the one mesothelioma case who had eight years on that job and also developed asbestosis and the one peritoneal mesothelioma case who also developed asbestosis and had six years of exposure milling/ fiberizing, Of the three pleural mesotheliomas with less than four years exposure two worked in milling/ fiberizing and the third case with four months of exposure had both asbestosis and a pleural mesothelioma indicating a significant cumulative exposure

during his brief period of time in the factory. Riebeckite (crocidolite) asbestos was never used in the fabrication of the commercial products but had been evaluated experimentally from time to time to when it was under consideration for use in a commercial product the Uxbridge factory might develop. Acheson et al. (1984) reports the mortality experience for a cohort of 5,969 men fabricating asbestos containing insulation board from 1947 to 1979. By the end of 1980 the cohort experienced 422 (7%) mortality. Only 4,280 men worked making asbestos insulation board with only 14% of these starting works prior to 1960. The other 1,689 workers made non-asbestos building materials in the same building complex. No additional mesotheliomas were reported besides the 5 reported earlier (Acheson et al., 1981). A 2-fold excess of lung cancer was report with 57 observed while only 29 were expected with increased lung cancer mortality for those starting work both before and after 1960 (Table 1). The asbestos exposed cohort also had 9 asbestosis deaths intermediate between Paterson and Tyler (Table 1). All the asbestosis cases had started work prior to the dust reduction in 1964 and 7 of the 9 started before 1960.

No large or significant excess from cancer at any other site was reported including gastrointestinal cancer and non- Hodgkin's lymphomas. The excess mortality was limited to the lung and pleura with 61 deaths occurring where 28 excess lung cancers and 4 excess pleural mesotheliomas occurred. All of the excess lung cancer mortality occurred among the workers who were smokers or ex-smokers. The Uxbridge cohort had three excess lung cancer deaths for every asbestosis death which is the same as at Paterson while Tyler had almost 8 excess lung cancers for each asbestosis death. Among the other workers in the complex who did not work directly with asbestos, but did share some facilities and worked in close proximity, no mesotheliomas or increased mortality from lung cancer was found.

In addition to the mortality study a lung content study was done on 48 workers from the Uxbridge, UK (Gibbs et al., 1994). Asbestos fiber-types and concentration in the lung parenchyma were investigated in each individual and compared to the lung pathology in that case. Fourteen cases of lung cancer and five pleural mesotheliomas were identified among the 48 samples studied. Gibbs et al. (1994) is silent on the relationship between his cases and those mesothelioma cases described in Acheson et al. (1981). Analytical transmission electron microscopy was used for the lung content analysis. All fibers with 3:1 aspect ratios of any length were counted. Large amounts of grunerite asbestos (amosite) (mean = 785 million fibers per gram dried lung tissue) and relatively small amounts of chrysotile (mean = 12 million fibers per gram dried lung tissue) were consistently found strengthening Acheson et al. (1981) claim the mesothelioma were caused by grunerite asbestos (amosite). The grunerite asbestos (amosite) concentration in the 14 lung cancers was 40% higher than in the five mesothelioma cases. A definite dose-response was demonstrated between grunerite asbestos (amosite) concentrations in the lung parenchyma and lung cancer and mesothelioma. Mesothelioma cases contained more grunerite asbestos (amosite) than the remaining cases without malignant disease.

The degree of interstitial fibrosis and number of asbestos bodies were graded. A positive relationship was found between the concentration of grunerite asbestos (amosite) and the grade of fibrosis and asbestos bodies. The observation indicates the exposure to grunerite asbestos (amosite) were the cause of the asbestosis rather than the chrysotile asbestos exposures. Duration of exposure affected the grades of fibrosis and asbestos bodies to a lesser extent. Chrysotile asbestos concentrations did not seem to affect the grades, perhaps owing to its relatively small amounts.

Eleven subjects, including one of the mesothelioma cases, had significant amounts of riebeckite (crocidolite) asbestos in their lungs. This could have been acquired outside this plant.

Grunerite asbestos (amosite) concentration in lung parenchyma examined verified the high level of exposure to this asbestos fiber-type in the factory.

7. Conclusions

The epidemiology studies of the three factories producing grunerite asbestos (amosite) products provide consistent evidence for this asbestos fiber-type producing asbestosis and increased risk of lung cancer and mesothelioma in both the pleura and peritoneum (Table 1). The highest mortality from asbestosis and peritoneal mesothelioma was in the cohort exposed in Paterson, NJ indicating it is likely to have the highest cumulative asbestos exposure of the three grunerite asbestos (amosite) exposed cohorts (Table 1). The results of the air sampling in the Tyler TX factory found the mean asbestos exposures associated with milling/fiberising to be 91.4f/mL. The other four jobs for which exposure information was gathered at Tyler also indicate the workers were receiving high asbestos exposures (Table 2). The increased risk of asbestos related disease after brief exposure in all these factories may be related to the very high exposures.

In all three factories pleural mesotheliomas did occur in workers with exposures of less than one year and one pleural mesothelioma occurred in a worker from Tyler and another from Uxbridge with less than six months exposure. The peritoneal mesothelioma cases are generally associated with higher cumulative exposures. Exposure conditions in all three factories appear to be rather similar and, it is possible, accumulated a 45f/mL year exposure history in as little as six months, significantly increasing the risk of pleural mesothelioma in all three cohorts.

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Figure 1 Timeline for asbestos-related mesothelioma at the factories using predominantly, if not exclusively, grunerite (amosite) asbestos: Paterson NJ, Tyler TX and Uxbridge UK.

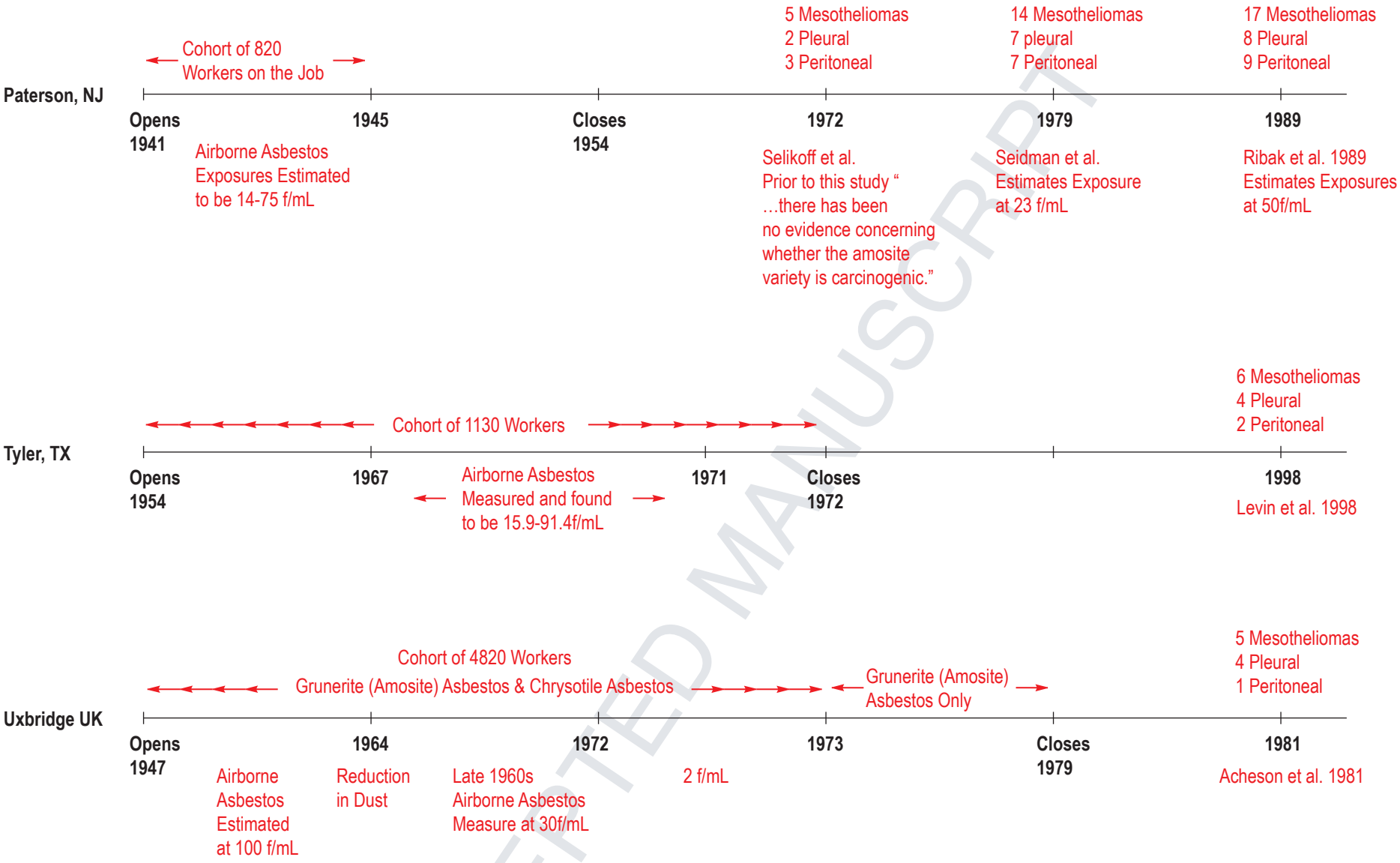

Table 1: Summary of the mortality experience of three populations occupationally exposed to grunerite (amosite) asbestos.
All three groups are thought to have been exposed predominately, if not excusively, to grunerite (amosite) asbestos.

Cohort Studied (Reference)	N° in Cohort	Deaths	N° of Lung Cancers	% of Lung Cancer	N° of Mesothelioma Deaths	Ratio†	% of Mesothelioma Deaths	N° of Asbestosis Cases	Asbestosis as a % of Mortality
Paterson, NJ (1)	230	105	25	23.8	5	2 to 3	4.8	14	13.3
Workers (2)	820	523	93	17.8	14	7 to 7	2.7	30	5.7
3	820	593	111	18.7	17	8 to 9	2.9	31	5.2
4	820	740	NR*	NR*	17	8 to 9	2.3	NR*	NR*
Tyler, TX(5) Workers	1130	222	35	15.8	6	4 to 2	2.7	3	1.4
Uxbridge, UK Workers (6,7)	4,820	333	57	17.1	5	4 to 1	1.5	9	2.7

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(7) Acheson ED, Gardiner MJ, Winter PD, Bennet C (1984) Cancer in a Factory Using Amosite Asbestos International Journal of Epidemiology 13: 3-10.
† Ratio of Pleural to Peritoneal

Table 2 Results of personal air sampling for five different jobs at the grunerite (amosite) asbestos factory in Tyler, Texas.The samples were analyze by phase-contrast light microscopy and the number of fiber per milliliter equal to or greater than 5µm with an aspect ratio of 3 to 1 or greater . are reported

Operation	1967	1970	1971	Mean for 3 Years
	fiber/mL			fibers/mL
Milling/Fiberizing	163.5	36.2	74.4	91.4
Forming	33.3	25.7	50.6	36.5
Curing	2.5	31	14.4	15.9
Finishing	44.6	34.8	39.5	39.6
Packing	16.7	17.9	22.8	19.1